CLAIMS

1. A method for screening modulators of mitochondrial function comprising adding a compound to be tested in a purified, isolated mitochondria preparation and simultaneously using fluorimetric analysis of mitochondrial morphology, and especially real-time fluorimetric analysis, combining analysis of morphometric parameters (SSC/FSC parameters) with analysis of membrane integrity by dye fluorescence.

2. The method of claim 1, wherein the analysis of the membrane integrity is performed using the JC-1 dye to characterize mitochondrial transmembrane potential $\Delta\psi m$ and study any change of the mitochondrial membrane permeability.

3. The method of claim 1 or 2, wherein the mechanism of mitochondrial membrane permeabilization is further characterized using pharmacological inducers or modulators of mitochondrial permeability such as Calcium, CCCP, Alamethicin, Bongkrekic acid, ruthenium red, cyclosporin A, DIDS.

4. The method of anyone of claims 1 to 3, further comprising studying endogenous or xenogenic mitochondrial regulators such as Bcl-2 family members and respiratory inhibitors on PTP-related MMP.

5. The method of anyone of claims 1 to 3, further comprising identifying compounds inducing MMP or preventing MMP induced by other agents, alone or in combination.

6. The method of anyone of claims 1 to 5, further comprising designing and defining new agents aiming at modulating MMP.

7. The method of anyone of claims 1 to 6, further comprising defining and manufacturing reagents or kits of reagent to put the method in use.

8. The method according to anyone of claims 1 to 4, further comprising characterizing mitochondrial reactivity in specific mitochondria, to be used to ascertain mitochondrial function in mitochondria from various tissues of physiological or pathological status, or pathology sources such as tumors.

9. The method according to anyone of claims 1 to 4, further comprising the diagnosis or characterization of mitochondrial function in patients with diseases, and especially genetic diseases or metabolic diseases.

10. Agents identified by using method according to claims 1 to 4, and shown to be able to modulate MMP on isolated mitochondria.

11. Peptides according to claim 10, having MMP modulating potency, selected in the group comprising:

ATLSALLAALRRIQRA	(SEQ ID N°1)
RKKRRQRRRGGATLSALLAALRRIQRA	(SEQ ID N°2)
RKKRRQRRRCGGLETRTETWMSSEGAWKQIQKVETWALRH	(SEQ ID N°3)
RKKRRQRRRCGGLANKKGAWLDSTKATRYLVKTESWILRN	(SEQ ID N°4)
GG*CRGDMFG*CGGLLFIHFRIGSRHSRIG	(SEQ ID N°5)
RIEIWILRH	(SEQ ID N°6)
RIAIWILRH	(SEQ ID N°7)
RKKRRQRRRGGRIEIWILRH	(SEQ ID N°8)
RKKRRQRRRGGRIAIWILRH	(SEQ ID N°9)
EHWSYWLRPGGGLLFIHFRIGCRHSRIG	(SEQ ID N°10)
EHWSYWLRPGGGGGSLLFIHFRIGCRHSRIG	(SEQ ID N°11)

and their derivatives.

Said peptides advantageously comprise in the C-terminal and N terminal position a stabilizing group such as an amide alkyl or acyl group and a marker or linking group, such as the biotinyl group. They can also include L- or D- aminoacids retro-inverso, reduced peptidic backbone, or being translated into pseudo peptides.

The invention also relates to said peptides bound to a peptidic delivery system, and optionally comprising a linker between said peptides and delivery system. This peptidic delivery system could advantageously being an extra cellular or intracellular targeting sequence, an antibody or a fragment thereof (ScFv). The linker can be a sequence allowing the peptide to adopt an helical structure independently of the peptidic delivery system, and can be formed by 2 to 6 aminoacids such as alanine or glycine, or a disulfide bridge,

or any such means as known by a man skilled in the art considering the state of the art knowledge. Said peptide could also be modified by insertions, deletions or mutations which conserve mitochondrial modulation potency.

12. Petides obtained by anology to peptides described in claim 11, presenting features characteristics of a MMP modulating function, defined as:

- containing at least 8 amino acids, and up to 50 amino acids
- at least a part of the peptide structure is an amphipathic alpha helix,
- 2, 3 or 4 amino acids are positively charged (lysine [K] or arginine [R]) and are located on the same side of the helix,
- when the helix is projected using helical wheel representation, the R and/or K amino acids form a cluster (see figure 15),
- when added to purified, isolated, mitochondria they induce changes (ultrastructural or membrane permeability).

Example of such peptides are selected below :

RKKRRQRRRGGGAWKHAQRIEIWILRH (SEQ ID N°12)
RKKRRQRRRGGGAWKHAQRIETWILRH (SEQ ID N°13)
RKKRRQRRRGGGAWKHAQRVESWILRN (SEQ ID N°14)
RKKRRQRRRGGGAWKRACRMETWILRH (SEQ ID N°15)
RKKRRQRRRGGGAWKQIQKVETWALRH (SEQ ID N°16)
RKKRRQRRRGGGAWRQVEKVETWALRH (SEQ ID N°17)
RKKRRQRRRGGGAWKHAQRIAIWILRH (SEQ ID N°18)
AWKHAQRIAIWILRH (SEQ ID N°19)
GG*CRGDMFG*CGGRIEIWILRH (SEQ ID N°20)
GG*CRGDMFG*CGGRIAIWILRH (SEQ ID N°21)
GG*CGRGDSPG*CGGRIEIWILRH (SEQ ID N°22)
GG*CGRGDSPG*CGGRIAIWILRH (SEQ ID N°23)

Where *C = cysteine engaged in cycling disulfide bridge

EHWSYWLRPGGGRIEIWILRH (SEQ ID N°24)
EHWSYWLRPGGGRIAIWILRH (SEQ ID N°25)

EHWSYWLRPGGGGGSRIEIWILRH (SEQ ID N°26)
EHWSYWLRPGGGGGSRIAIWILRH (SEQ ID N°27)
EHWSYWLRPGGGGGSGAWKHAQRIEIWILRH (SEQ ID N°28)
EHWSYWLRPGGGGGSGAWKHAQRIAIWILRH (SEQ ID N°29)
EHWSYWLRPGGGLLFIHFKIGCKHSKIG (SEQ ID N°30)
EHWSYWLRPGGGGGSLLFIHFKIGCKHSKIG (SEQ ID N°31)
EHWSYWLRPGGGLLFIHFRIGSRHSRIG (SEQ ID N°32)
EHWSYWLRPGGGGGSLLFIHFRIGSRHSRIG (SEQ ID N°33)
EHWSYWLRPGGGLLFIHFKIGSKHSKIG (SEQ ID N°34)
EHWSYWLRPGGGGGSLLFIHFKIGSKHSKIG (SEQ ID N°35)

in which the W6 residue can be replaced by the D-aminoacid $_{d}$W. These peptide are claimed along with their derivatives as dezfined in claim 10.